Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1-11. (cancelled)

12. (currently amended) A method for the production of recombinant heterologous protein in prokaryotic cells comprising.

expressing a vector in said prokaryotic cells said vector comprising:

(a) DNA encoding an OmpA signal peptide (SEQ ID NO:1);

(b) DNA encoding said heterologous protein; and

(c) DNA encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3);

wherein said DNA of (a) is located upstream of said DNA of (c), and said DNA of (b) is located downstream of said DNA of (c);

wherein said DNAs of (a), (b), and (c) are operably linked; and

~~expressing a vector in said prokaryotic cells which comprises DNA encoding said heterologous protein operably linked to DNA encoding the OmpA signal peptide (SEQ ID NO:1);~~

~~wherein said DNA sequence encoding said OmpA signal peptide is operatively linked to a nucleic acid sequence encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3); and~~

wherein said heterologous protein is secreted extracellularly as an active protein.

13. (previously presented) The method according to claim 12, wherein said heterologous protein is secreted as a correctly folded protein.

14. (currently amended) The method according to claim 12, wherein said DNA of (c) ~~nucleic acid sequence~~ encodes the peptide SEGN (SEQ ID NO:2).

15. (currently amended) The method according to claim 14, wherein said DNA of (c) is ~~nucleic acid sequence comprises~~ TCTGAGGGAAAC (SEQ ID NO:4).

16. (currently amended) The method according to claim 12, wherein said DNA of (c) is ~~nucleic acid sequence comprises~~ encodes the peptide SEGNSD (SEQ ID NO:3).

17. (currently amended) The method according to claim 16, wherein said DNA of (c) is ~~nucleic acid sequence comprises~~ TCTGAGGGAAACAGTGAC (SEQ ID NO:5).

18. (previously presented) The method according to claim 12, wherein the prokaryotic cell is *E. coli*.

19. (currently amended) A method for the production of recombinant heterologous protein in prokaryotic cells comprising:

a) amplifying DNA encoding said heterologous protein by PCR;

b) purifying the PCR product;

c) inserting said PCR product into a vector, wherein said vector comprises:

(a) DNA encoding an OmpA signal peptide (SEQ ID NO:1);

(b) DNA encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3); and

(c) DNA encoding gpIII;

wherein said DNA of (a) is located upstream of said DNA of (b); wherein said PCR product is located downstream of said DNA of(b) and upstream of said DNA of (c); and

wherein said DNA of (c) is located downstream of said PCR product;

wherein said DNAs of (a), (b), and (c) and said PCR product are operably linked;

~~wherein said vector comprises a DNA encoding an OmpA signal peptide, a peptide selected from the group consisting of SEGN (SEQ ID NO: 2) and SEGNSD (SEQ ID NO:3), and DNA encoding gpIII; and~~

~~wherein said PCR product is operably linked downstream to the DNA encoding the OmpA signal peptide and operably linked upstream to the DNA encoding gpIII of said vector;~~

d) inserting a stop codon between the heterologous protein and gpIII; and

e) expressing ~~a~~said vector of step (c) in the prokaryotic cells.

20. (previously presented) The method according to claim 19, further comprising:

f) purifying said heterologous protein.

21. (currently amended) The method according to claim 12, wherein the heterologous protein is tissue plasminogen activator ~~or a fragment thereof~~.

22-25. (cancelled)

26. (previously presented) The method according to claim 12, wherein the vector is a phagemid vector comprising DNA coding for OmpA signal peptide (SEQ ID NO:1) and DNA coding for gpIII.

27. (currently amended) The method according to claim 12, wherein the vector comprises the pComb3HSS phagemid vector.

28. (previously presented) The method according to claim 12, wherein the DNA sequence of OmpA comprises ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG TG GCCCAGGCGGCC (SEQ ID NO:1).

29. (previously presented) The method according to claim 12, wherein the DNA sequence of OmpA consists of ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG TG GCCCAGGCGGCC (SEQ ID NO:1).

30. (previously presented) The method according to claim 12, wherein the DNA of the heterologous protein is preceded by a lac promoter and/or a ribosomal binding site.

31. (currently amended) A method for the production of recombinant heterologous proteintissue plasminogen activator in prokaryotic cells comprising:

expressing a vector in said prokaryotic cells, said vector comprising:

(a) DNA encoding an OmpA signal peptide (SEQ ID NO:1);

(b) DNA encoding the heterologous proteintissue plasminogen activator; and

(c) DNA encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3);

wherein said DNA of (a) is located upstream of said DNA of (c), and said DNA of (b) is located downstream of said DNA of (c); and

wherein said DNAs of (a), (b), and (c) are operably linked;

~~expressing a vector in said prokaryotic cells which comprises DNA encoding said tissue plasminogen activator operably linked to DNA encoding the OmpA signal peptide (SEQ ID NO:1);~~

wherein the heterologous protein is a K2S variant; and

wherein the heterologous protein ~~said tissue plasminogen activator (tPA)~~is secreted extracellularly as an active protein.

32. (currently amended) The method according to claim 31, wherein said heterologous protein ~~said tissue plasminogen activator~~ is secreted as a correctly folded protein.

33-34. (cancelled)

35. (currently amended) The method according to claim 31[[34]], wherein said DNA of (b) ~~nucleic acid sequence~~ encodes the peptide SEGN (SEQ ID NO:2).

36. (currently amended) The method according to claim 35, wherein said DNA of (b) is ~~nucleic acid sequence comprises~~ TCTGAGGGAAAC (SEQ ID NO:4).

37. (currently amended) The method according to claim 31[[34]], wherein said DNA of (b) ~~nucleic acid sequence~~ encodes the peptide SEGNSD (SEQ ID NO:3).

38. (currently amended) The method according to claim 37, wherein said DNA of (b) is ~~nucleic acid sequence comprises~~ TCTGAGGGAAACAGTGAC (SEQ ID NO:5).

39. (previously presented) The method according to claim 31, wherein the prokaryotic cell is *E. coli*.

40. (currently amended) A method for the production of recombinant heterologous protein~~tissue plasminogen activator~~ in prokaryotic cells comprising:

a) amplifying DNA encoding said heterologous protein~~tissue plasminogen activator~~ by PCR;

b) purifying the PCR product;

c) inserting said PCR product into a vector,

wherein said vector comprises:

(a) DNA encoding an OmpA signal peptide (SEQ ID NO:1);

(b) DNA encoding a peptide selected from the group consisting of SEGN (SEQ ID NO:2) and SEGNSD (SEQ ID NO:3); and

(c) DNA encoding gpIII;

wherein said DNA of (a) is located upstream of said DNA of (b); wherein said PCR product is located downstream of said DNA of (b) and upstream of said DNA of (c); and

wherein said DNA of (c) is located downstream of said PCR product;

wherein said DNAs of (a), (b), and (c) and said PCR product are operably linked;

~~wherein said vector comprises a DNA encoding an OmpA signal peptide and DNA encoding gpIII; and~~

~~wherein said PCR product is operably linked downstream to the DNA encoding the OmpA signal peptide and operably linked upstream to the DNA encoding gpIII of said vector~~;

d) inserting a stop codon between the heterologous protein and gpIII; and

e) expressing ~~a~~said vector of step (c) in the prokaryotic cells;

wherein the heterologous protein is a K2S variant.

41. (previously presented) The method according to claim 40, further comprising:

f) purifying said heterologous protein.

42-45. (cancelled)

46. (currently amended)~~The method according to claim 44, wherein said variant is the K2S variant of tissue plasminogen activator~~ A method for the production of recombinant K2S in prokaryotic cells comprising:

expressing a vector in said prokaryotic cells, said vector comprising:

(a) DNA encoding an OmpA signal peptide (SEQ ID NO:1); and

(b) DNA encoding K2S;

wherein said DNA of (a) is located upstream of said DNA of (b); and

wherein said DNAs of (a) and (b) are operably linked;

wherein the K2S is secreted extracellularly as an active protein.

47. (cancelled)

48. (currently amended) The method according to claim 31, wherein the vector is a phagemid vector comprising DNA coding for OmpA signal peptide (SEQ ID NO:1) and the peptide SEGN (SEQ ID NO: 2) or the peptide SEGNSD (SEQ ID NO:3~~DNA coding for gpIII~~.

49. (currently amended) The method according to claim 48, wherein the phagemid vector further comprises DNA coding for gpIII~~the peptide SEGN (SEQ ID NO: 2) or the peptide SEGNSD (SEQ ID NO:3)~~.

50. (currently amended) The method according to claim 31, wherein the vector comprises the pComb3HSS phagemid vector.

51. (previously presented) The method according to claim 31, wherein the DNA sequence of OmpA comprises ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG TG GCCCAGGCGGCC (SEQ ID NO:1).

52. (previously presented) The method according to claim 31, wherein the DNA sequence of OmpA consists of ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGTTTCGCTACCG TG GCCCAGGCGGCC (SEQ ID NO:1).

53. (currently amended) The method according to claim 31, wherein the DNA encoding K2S~~of the heterologous protein~~ is preceeded by a lac promotor and/or a ribosomal binding site.

54. (new) The method of claim 31, wherein the K2S variant is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 and SEQ ID NO:17.

55. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:10.

56. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:11.

57. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:12.

58. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:13.

59. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:14.

60. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:15.

61. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:16.

62. (new) The method of claim 54, wherein the K2S variant is SEQ ID NO:17.

63. (new) The method of claim 40, wherein the K2S variant is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16 and SEQ ID NO:17.

64. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:10.

65. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:11.

66. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:12.

67. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:13.

68. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:14.

69. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:15.

70. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:16.

71. (new) The method of claim 63, wherein the K2S variant is SEQ ID NO:17.